******* INVENTOR RESULTS *******

```
=> d his l70

     (FILE 'HCAPLUS' ENTERED AT 10:07:26 ON 31 OCT 2007)
L70            1 S L69 NOT L62

=> d que l70
L2             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  DICLAZURIL/CN
L3             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  101831-37-2
L4             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 OR L3
L5             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ETHANOL/CN
L6             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  64-17-5/RN
L7             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 OR L6
L8             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SODIUM HYDROXIDE/CN
L9             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  64-17-5/RN
L10            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 OR L9
L11            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ETHANOLAMINE/CN
L12            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  141-43-5 /RN
L13            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L11 OR L12
L16            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  N-METHYLGLUCAMINE/CN
L17            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  6284-40-8/RN
L18            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 OR L17
L20          143 SEA FILE=HCAPLUS ABB=ON   PLU=ON  DICLAZURIL/BI
L21          154 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L20 OR L4
L22       284893 SEA FILE=HCAPLUS ABB=ON   PLU=ON  ETHANOL/BI
L23       332305 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L22 OR L7
L24         2847 SEA FILE=HCAPLUS ABB=ON   PLU=ON  (PEG(W)400 OR PEG400 OR
                 PEG-400 OR POLYETHYLENEGLYCOL(W)400)/BI
L29          509 SEA FILE=HCAPLUS ABB=ON   PLU=ON  N/OBI(W)METHYLGLUCAMINE/BI
L30        99844 SEA FILE=HCAPLUS ABB=ON   PLU=ON  SODIUM HYDROXIDE/BI
L31        26353 SEA FILE=HCAPLUS ABB=ON   PLU=ON  ETHANOLAMINE/BI
L33         1528 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L29 OR L18
L34       325195 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L10 OR L30
L35        41162 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L13 OR L31
L36          701 SEA FILE=HCAPLUS ABB=ON   PLU=ON  ANTI/OBI(W)PROTOZOAL?/OBI OR
                 ANTIPROTOZOAL?/OBI
L37         4809 SEA FILE=HCAPLUS ABB=ON   PLU=ON  (PROTOZOAL/OBI OR CENTRAL
                 NERVOUS SYSTEM?/OBI OR CNS/OBI OR CEREBRAL PROTOZOAL/OBI) (W)
                 (INFECT?/OBI OR DISEASE?/OBI)
L38          210 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L36 (L) (AGENT?/OBI)
L39            9 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L21 AND (L36 OR L37 OR L38)
L40           11 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L21 AND (L23 OR L24)
L43           10 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L21 AND (L33 OR L34 OR L35)
L45            3 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L39 (L) (L40 OR L43)
L47         4034 SEA FILE=HCAPLUS ABB=ON   PLU=ON  PROTOZOACIDE?/BI
L49       156714 SEA FILE=HCAPLUS ABB=ON   PLU=ON  ALCOHOLS/CT
L50        29739 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L49 (L) (THU OR BIOL)/RL
L51        60391 SEA FILE=HCAPLUS ABB=ON   PLU=ON  SOLVENTS/CT
L55           46 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L47 AND L50
L56            7 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L55 AND L51
L58        45011 SEA FILE=HCAPLUS ABB=ON   PLU=ON  EMULSIFIER?/BI
L59            2 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L56 AND L58
L60            1 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L56 AND (L36 OR L37)
L61            2 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L59 OR L60
L62            4 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L45 OR L61
L63           43 SEA FILE=HCAPLUS ABB=ON   PLU=ON  ("DE SPIEGELEER B"/AU OR "DE
                 SPIEGELEER B M"/AU OR "DE SPIEGELEER B M J"/AU OR "DE SPIEGELEE
                 R BART"/AU OR "DE SPIEGELEER BART M J"/AU)
L64           24 SEA FILE=HCAPLUS ABB=ON   PLU=ON  ("DOSOGNE H"/AU OR "DOSOGNE
                 HILDE"/AU)
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```
L65           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L63 AND L64
L66          65 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L63 OR L64
L67           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L66 AND (L36 OR L37)
L68           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L66 AND L21
L69           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 OR L67 OR L68
L70           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L69 NOT L62


=> d his l109

     (FILE 'WPIX' ENTERED AT 10:56:22 ON 31 OCT 2007)
L109          3 S L107 OR L108
                SAVE TEMP L109 JAV162WPIN/A

     FILE 'STNGUIDE' ENTERED AT 10:58:37 ON 31 OCT 2007

=> d que l109
L96          68 SEA DE SPIEGELEER B/AU
L97          14 SEA DE SPIEGELEER BART/AU
L98          12 SEA DOSOGNE HILDE/AU
L99          60 SEA DOSOGNE H/AU
L107          3 SEA FILE=WPIX ABB=ON  PLU=ON  L96 OR L97
L108          1 SEA FILE=WPIX ABB=ON  PLU=ON  L98 OR L99
L109          3 SEA FILE=WPIX ABB=ON  PLU=ON  L107 OR L108


=> d his l106

     (FILE 'MEDLINE, BIOSIS, BIOTECHNO, DRUGU, EMBASE' ENTERED AT 10:52:07 ON
     31 OCT 2007)
L106         12 S L101 OR L105

=> d que l106
L97          14 SEA DE SPIEGELEER BART/AU
L98          12 SEA DOSOGNE HILDE/AU
L101          1 SEA L97 AND L98
L102         25 SEA L97 OR L98
L105         11 SEA L102 AND (PHARMAC? OR THERAP? OR TREAT?)
L106         12 SEA L101 OR L105


=> dup rem l70 l106 l109
FILE 'HCAPLUS' ENTERED AT 11:03:55 ON 31 OCT 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE 'MEDLINE' ENTERED AT 11:03:55 ON 31 OCT 2007

FILE 'BIOSIS' ENTERED AT 11:03:55 ON 31 OCT 2007
Copyright (c) 2007 The Thomson Corporation

FILE 'WPIX' ENTERED AT 11:03:55 ON 31 OCT 2007
COPYRIGHT (C) 2007 THE THOMSON CORPORATION
PROCESSING COMPLETED FOR L70
PROCESSING COMPLETED FOR L106
PROCESSING COMPLETED FOR L109
L110         13 DUP REM L70 L106 L109 (3 DUPLICATES REMOVED)
                ANSWER '1' FROM FILE HCAPLUS
                ANSWERS '2-7' FROM FILE MEDLINE
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ANSWERS '8-10' FROM FILE BIOSIS
ANSWERS '11-13' FROM FILE WPIX

=> d l110 1-13 ibib ab

L110 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2007:1192392 HCAPLUS Full-text
TITLE: Bovine blood neutrophil acyloxyacyl hydrolase (AOAH) activity during endotoxin and coliform mastitis
AUTHOR(S): Mehrzad, Jalil; **Dosogne, Hilde**; **De Spiegeleer, Bart**; Duchateau, Luc; Burbenich, Christian
CORPORATE SOURCE: Faculty of Veterinary Medicine, Department of Pathobiology, Section Immunology, Ferdowsi University of Mashhad, Mashhad, Iran
SOURCE: Veterinary Research (2007), 38(5), 655-668
CODEN: VEREEM; ISSN: 0928-4249
PUBLISHER: EDP Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The dynamics of blood neutrophil acyloxyacyl hydrolase (AOAH) activity, the appearance of endotoxin (lipopolysaccharide, LPS) in blood and the role of blood neutrophil AOAH in the severity of Escherichia coli and endotoxin mastitis were investigated in early postpartum dairy cows exptl. challenged with either endotoxin (n = 6) or E. coli (n = 6). The AOAH activity of blood neutrophils started to decrease significantly at post challenge hours (PCH) 6-24 and 12-24 in the endotoxin and E. coli-challenged groups, resp.; it returned to pre-challenged values at PCH 48 in both endotoxin- and E. coli-challenged groups. The cows were classified as moderate and severe responders according to milk production loss in the non-challenged quarters at PCH 48. There were no severe responders in the endotoxin-challenged group. In the E. coli-challenged group, only 1 severe responder was identified. The pre-challenge neutrophil AOAH activity of the severe responder was .apprx.30% lower than that of moderate responders. No LPS was detected in the plasma of endotoxin-challenged cows; neither was it found in the plasma of moderate responders in the E. coli-challenged group at any PCH. However, at PCH 6, a remarkable amount of LPS was detected in the plasma of the severe responder from the E. coli-challenged group. Furthermore, neutrophil AOAH activity was increased by .apprx.70% in the severe responder at PCH 6, but it increased by only .apprx.15% in moderate responders. This was followed by a decreased neutrophil AOAH activity at PCH 12-24 and 24-72 in moderate and severe responders, resp.; the decreased AOAH activity at those PCH was more pronounced in the severe responder. The pronounced decreased neutrophil AOAH activity during mastitis often coincided with extreme leukopenia, neutropenia and a maximal number of immature neutrophils in the blood. Our results demonstrate that a decrease in neutrophil AOAH activity results in the appearance of LPS in the blood, and low blood neutrophil deacylation activity could be considered as a risk factor for severe clin. coliform mastitis.

L110 ANSWER 2 OF 13 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2006073207 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16459267
TITLE: Influence of sedation and data acquisition method on tracer uptake in animal models: [123I]-2-iodo-L-phenylalanine in pentobarbital-sedated tumor-bearing athymic mice.
AUTHOR: Kersemans Veerle; **De Spiegeleer Bart**; Mertens John; Slegers Guido
CORPORATE SOURCE: Laboratory for Radiopharmacy, Universiteit Gent, Belgium.. veerle.kersemans@utoronto.ca

SOURCE: Nuclear medicine and biology, (2006 Jan) Vol. 33, No. 1, pp. 119-23.
Journal code: 9304420. ISSN: 0969-8051.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200606
ENTRY DATE: Entered STN: 7 Feb 2006
Last Updated on STN: 20 Jun 2006
Entered Medline: 19 Jun 2006

AB OBJECTIVES: To minimize movement artifacts during tracer imaging studies, the animals are generally sedated. Although many reports describe the effect of barbiturates on brain function, less is published about the general impact on the extracerebral metabolism and tracer biodistribution. This report describes the influence of pentobarbital on tumor uptake of [(123)I]-2-iodo-L-phenylalanine ([(123)I]-2I-L-PA) using dissection and nuclear imaging. METHODS: R1M tumor-bearing athymic mice were divided into two populations: untreated and pentobarbital-**treated**. Each group was subjected to dynamic and static planar imaging and organ dissection after [(123)I]-2I-L-PA injection. Two-compartment blood modeling was performed. Analysis of variance (ANOVA), t test and clustered boxplot analyses were used to compare the results between the **treatment** groups and between the data acquisition methods. RESULTS: Two-compartment blood modeling demonstrated that pentobarbital decreased the elimination velocity and the distribution toward the peripheral compartment. Both observations lead to higher blood pool and kidney activities after administering pentobarbital. The dependence of the differential absorption/differential uptake ratio results on the factors organ, method and **treatment** (3-factor ANOVA) demonstrated that all factors had a significant effect. Moreover, a significant effect for method and **treatment** was observed for each individual organ, and the ratio of tumor to background showed additionally an ordinal interaction between the latter two factors. Although the tumor uptake values were lower when using sedation and nuclear imaging, the tumor could still be visualized. CONCLUSIONS: An effect of sedation **treatment** and data acquisition method was demonstrated for 2-iodo-phenylalanine, currently under development as tumor tracer. It is recommended that animal experiments should include quantitative investigation of sedation and the data acquisition method.

L110 ANSWER 3 OF 13 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002143268 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11873813
TITLE: Potential mechanism of action of J5 vaccine in protection against severe bovine coliform mastitis.
AUTHOR: **Dosogne Hilde**; Vangroenweghe Frederic; Burvenich Christian
CORPORATE SOURCE: Ghent University, Faculty of Veterinary Medicine, Department of Physiology, Biochemistry and Biometrics, Merelbeke, Belgium.
SOURCE: Veterinary research, (2002 Jan-Feb) Vol. 33, No. 1, pp. 1-12. Ref: 59
Journal code: 9309551. ISSN: 0928-4249.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 7 Mar 2002
Last Updated on STN: 19 Jun 2002
Entered Medline: 18 Jun 2002

AB Coliform mastitis is one of the most difficult diseases to **treat** in the modern dairy industry. Curative **therapy** with antibiotics remains only moderately effective and depends on the stage at which the disease is **treated.** The most successful strategies for combating coliform mastitis appear to be prevention by hygienic management or prophylactic immunization. The severity of clinical symptoms of coliform mastitis has been shown to be reduced by immunization with the Escherichia coli J5 vaccine. However, although the J5 vaccine has been licensed in the United States for about 10 years, the immunological basis of its mechanism of action is still unknown. Until now, protection by J5 vaccination has often been explained by a straightforward mechanism of enhanced antibody production resulting in increased opsonization of coliform bacteria and lipopolysaccharides (LPS). The possibility that J5 vaccination could decrease risk factors for coliform mastitis such as impaired blood polymorphonuclear neutrophil leukocyte (PMN) diapedesis has never been investigated. This review provides arguments to support the hypothesis that J5 vaccination may reduce the severity of coliform mastitis by inducing a condition of mammary gland hyper-responsiveness, characterized by a T helper 1 (Th1) response and mediated by memory cells inside the mammary gland, finally resulting in enhanced PMN diapedesis upon an intramammary infection.

L110 ANSWER 4 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2006440650 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16572305
TITLE: 123/125I-labelled 2-iodo-L: -phenylalanine and 2-iodo-D: -phenylalanine: comparative uptake in various tumour types and biodistribution in mice.
AUTHOR: Kersemans Veerle; Cornelissen Bart; Kersemans Ken; Bauwens Matthias; Dierckx Rudi A; **De Spiegeleer Bart**; Mertens John; Slegers Guido
CORPORATE SOURCE: Laboratory for Radiopharmacy, Universiteit Gent, Harelbekestraat 72, B-9000, Gent, Belgium.. veerle.kersemans@utoronto.ca
SOURCE: European journal of nuclear medicine and molecular imaging, (2006 Aug) Vol. 33, No. 8, pp. 919-27. Electronic Publication: 2006-03-30.
Journal code: 101140988. ISSN: 1619-7070.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200611
ENTRY DATE: Entered STN: 26 Jul 2006
Last Updated on STN: 19 Dec 2006
Entered Medline: 30 Nov 2006

AB PURPOSE: In vitro in the R1M cell model and in vivo in the R1M tumour-bearing athymic model, both [(123)I]-2-iodo-L: -phenylalanine and [(123)I]-2-iodo-D: -phenylalanine have shown promising results as tumour diagnostic agents for SPECT. In order to compare these two amino acid analogues and to examine whether the observed characteristics could be generalised, both isomers were evaluated in various tumour models. METHODS: Transport type characterisation in vitro in A549, A2058, C6, C32, Capan2, EF43fgf4, HT29 and R1M cells with [(123)I]-2-iodo-L: -phenylalanine was performed using the method described by Shotwell et al. Subsequently, [(123)I]-2-iodo-L: -phenylalanine and [(123)I]-

2-iodo-D: -phenylalanine tumour uptake and biodistribution were evaluated using dynamic planar imaging and/or dissection in A549, A2058, C6, C32, Capan2, EF43fgf4, HT29 and R1M inoculated athymic mice. Two-compartment blood modelling of the imaging results was performed. RESULTS: In vitro testing demonstrated that [(123)I]-2-iodo-L: -phenylalanine was transported in all tumour cell lines by LAT1. In all tumour models, the two amino acid analogues showed the same general biodistribution characteristics: high and specific tumour uptake and renal tracer clearance. Two-compartment modelling revealed that the D: -isomer showed a faster blood clearance together with a faster distribution to the peripheral compartment in comparison with [(123)I]-2-iodo-L: -phenylalanine. CONCLUSION: [(123)I]-2-iodo-L: -phenylalanine and its D: -isomer are promising tumour diagnostic agents for dynamic planar imaging. They showed a high and similar uptake in all tested tumours. [(123)I]-2-iodo-D: -phenylalanine showed better tracer characteristics concerning radiation dose to other organs.

L110 ANSWER 5 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2006494172 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16918300
TITLE: Optimization by experimental design of precursor synthesis and radiolabeling of 2-iodo-L-phenylalanine, a novel amino acid for tumor imaging.
AUTHOR: Kersemans Veerle; Kersemans Ken; Cornelissen Bart; Staelens Ludovicus; **de Spiegeleer Bart**; Mertens John; Slegers Guido
CORPORATE SOURCE: Laboratory of Radiopharmacy, Universiteit Ghent, Ghent, Belgium.. Veerle.Kersemans@utoronto.ca
SOURCE: Cancer biotherapy & radiopharmaceuticals, (2006 Jun) Vol. 21, No. 3, pp. 235-42.
Journal code: 9605408. ISSN: 1084-9785.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200701
ENTRY DATE: Entered STN: 22 Aug 2006
Last Updated on STN: 12 Jan 2007
Entered Medline: 11 Jan 2007

AB Various radiolabeled amino acids show promising results in tumor detection, as applied in the management of cancer patients. We synthesized the precursor 2-iodo-L-phenylalanine for easier kit labeling of [123/125I]- 2-iodo-L-phenylalanine, using the Cu1+ -assisted nucleophilic halogen exchange. Precursor synthesis was optimized by experimental design: Eight parameters were initially screened by a quarter fractional design. The resulting most important parameters (i.e., temperature, CuSO4, NaI) were further optimized using a full three-factor, three-level factorial design. The final conclusion for the optimal values for temperature, reaction time, and concentration of 2-bromo-L- phenylalanine, NaI, CuSO4, SnSO4, C6H6O7, and C7H6O4 were 180 degrees C, 24 hours, 61 mM, 485 mM, 10 mM, 90 mM, 90 mM, and 100 mM, respectively. The yield was increased from 39% to consistently more than 74% 2-iodo-L-phenylalanine. Structure confirmation and quality control was performed by 1H-NMR, mass spectroscopy (MS), and high-performance liquid chromatography (HPLC) (reverse phase [RP] and chiral). No phenylalanine-related impurities or racemization was detected. Subsequent radioiodination of the obtained 2-iodo-L-phenylalanine was performed in kit conditions with n.c.a. Na123/125I, resulting in a labeling yield of > 98%. After Ag-membrane filtration, a radiochemical purity of > 99% was obtained. The Cu1+ -assisted nucleophilic exchange reaction allows both routine kit preparation and "cold" synthesis of

2-iodo-L-phenylalanine from 2-bromo-L-phenylalanine. The reaction presents an interesting alternative for a cumbersome multistep, stereo-specific synthesis.

L110 ANSWER 6 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2006073206 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16459266
TITLE: Comparative biodistribution study of the new tumor tracer [123I]-2-iodo-L-phenylalanine with [123I]-2-iodo-L-tyrosine.
AUTHOR: Kersemans Veerle; Cornelissen Bart; Kersemans Ken; Dierckx Rudi A; **De Spiegeleer Bart**; Mertens John; Slegers Guido
CORPORATE SOURCE: Laboratory for Radiopharmacy, Universiteit Ghent, Belgium.. veerle.kersemans@ugent.be
SOURCE: Nuclear medicine and biology, (2006 Jan) Vol. 33, No. 1, pp. 111-7.
Journal code: 9304420. ISSN: 0969-8051.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200606
ENTRY DATE: Entered STN: 7 Feb 2006
Last Updated on STN: 20 Jun 2006
Entered Medline: 19 Jun 2006

AB INTRODUCTION: Both A- and l-type amino acid transport are increased in tumor cells relative to normal tissue; these transport systems have been the major focus of the development of amino acid tumor tracers to overcome the limitations of [(18)F]-fluorodeoxyglucose ((18)F-FDG). The newly developed tracer 2-amino-3-(2-[(123)I]iodophenyl)propanoic acid ([(123)I]-2-iodo-l-phenylalanine) showed high and specific tumor uptake, slow renal elimination and low brain uptake. We compared [(123)I]-2-iodo-L-phenylalanine with 2-amino-3-(4-hydroxy-2- [(123)I]iodophenyl)propanoic acid ([(123)I]-2-iodo-L-tyrosine), an L-tyrosine analogue that has recently entered clinical trials. METHODS: [(123)I]-2-iodo-L-phenylalanine and [(123)I]-2-iodo-L-tyrosine were evaluated in rhabdomyosarcoma tumor-bearing athymic mice by means of dynamic planar imaging (DPI) and dissection. A displacement study with L-phenylalanine was performed to prove the specificity of tracer tumor uptake, and kinetic modeling was applied to the DPI results. Moreover, the biodistribution of both tracers was compared with that of (18)F-FDG. RESULTS: Both [(123)I]-2-iodo-L-phenylalanine and [(123)I]-2-iodo-L- tyrosine showed fast, high and specific tumor accumulation with no significant difference. However, [(123)I]-2-iodo-L-phenylalanine was cleared faster from the blood to the bladder in comparison with the tyrosine analogue. Moreover, [(123)I]-2-iodo-L-phenylalanine tumor uptake equilibrated faster with blood. Dissection showed that [(123)I]-2-iodo-L-tyrosine slightly accumulated in the liver, which was not the case for the phenylalanine analogue. In contrast to (18)F-FDG, both tracers showed low uptake in the heart and normal brain tissue, which is advantageous for tumor detection in these organs. CONCLUSIONS: [(123)I]-2-iodo-L-phenylalanine showed more promising characteristics for oncological imaging as compared with [(123)I]-2-iodo-L-tyrosine. The former tracer not only demonstrated faster blood clearance but also showed that the tracer uptake in the tumor reached its equilibrium with the blood pool activity faster, which led to faster and better tumor contrast. Moreover, both tracers could overcome an important limitation of (18)F-FDG-its high normal brain uptake.

L110 ANSWER 7 OF 13 MEDLINE on STN
ACCESSION NUMBER: 2005649579 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16330577
TITLE: In vivo evaluation and dosimetry of 123I-2-iodo-D-phenylalanine, a new potential tumor-specific tracer for SPECT, in an R1M rhabdomyosarcoma athymic mouse model.
AUTHOR: Kersemans Veerle; Cornelissen Bart; Bacher Klaus; Kersemans Ken; Thierens Hubert; Dierckx Rudi A; **De Spiegeleer Bart**; Slegers Guido; Mertens John
CORPORATE SOURCE: Laboratory for Radiopharmacy, Universiteit Gent, Gent, Belgium.. veerle.kersemans@utoronto.ca
SOURCE: Journal of nuclear medicine : official publication, Society of Nuclear Medicine, (2005 Dec) Vol. 46, No. 12, pp. 2104-11.
Journal code: 0217410. ISSN: 0161-5505.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200602
ENTRY DATE: Entered STN: 8 Dec 2005
Last Updated on STN: 28 Feb 2006
Entered Medline: 27 Feb 2006

AB Earlier reports described the preferential uptake of d-amino acids in tumor-bearing mice. Moreover, it was shown that in tumor cells in vitro the L-amino acid transporter system seemed to lack stereospecificity. Because of the successful results with 123/125I-2-iodo-L-phenylalanine, 123/125I-2-iodo-D-phenylalanine was developed, and its tumor-detecting characteristics were evaluated in vivo. METHODS: 123I labeling of 2-iodo-D-phenylalanine was performed with a kit formulation by use of Cu1+-assisted nucleophilic exchange. 123I-2-Iodo-D-phenylalanine was evaluated in R1M tumor-bearing athymic mice by dynamic planar imaging (DPI) and dissection. The in vivo stability of the tracer was tested by high-performance liquid chromatography. Tumor tracer retention and tracer contrast were evaluated as a function of time. Two-compartment blood modeling from DPI results and dosimetric calculations from biodistribution results were carried out. Moreover, 125I-2-iodo-D-phenylalanine and 18F-FDG uptake in acute inflammation was investigated. RESULTS: 123I-2-Iodo-D-phenylalanine was metabolically stable. Fast, high, and specific tumor retention was observed. Two-compartment modeling confirmed the fast clearance of the tracer through the kidneys to the bladder, as observed by DPI and dissection. Moreover, compared with the L-isomer, 123I-2-iodo-D-phenylalanine demonstrated faster clearance and faster uptake in the peripheral compartment. No accumulation in the abdomen or in the brain was noted. Dosimetry revealed that 123I-2-iodo-D- phenylalanine demonstrated a low radiation burden comparable to those of 123I-2-iodo-L-phenylalanine and 123I-2-iodo-L-tyrosine. Although 123I-2-iodo-D-phenylalanine showed a tumor retention of only 4%, the tumor contrast was increased up to 350% at 19 h after injection. CONCLUSION: 123I-2-Iodo-D-phenylalanine is a promising tracer for diagnostic oncologic imaging because of its high, fast, and specific tumor uptake and fast clearance from blood.

L110 ANSWER 8 OF 13 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:516049 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600509271
TITLE: Synthesis and HPLC-purification of [Br-77]TMC125-R165335 (etravirine), a new anti-HIV drug of the DAPY-NNRTI class.
AUTHOR(S): **De Spiegeleer, Bart** [Reprint Author]; Dumont, Filip; Peremans, Kathelijne; Burvenich, Christian; Van Vooren, Lieven; Rosier, Jan; Baert, Lieven; Wigerinck,

Piet; Slegers, Guido
CORPORATE SOURCE: Univ Ghent, DruQuaR Grp, Fac Pharmaceut Sci, Harelbekestr 72, B-9000 Ghent, Belgium
Bart.despiegeleer@ugent.be
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals, (JUL 2006) Vol. 49, No. 8, pp. 683-686.
CODEN: JLCRD4. ISSN: 0362-4803.
DOCUMENT TYPE: Article
Editorial
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Oct 2006
Last Updated on STN: 4 Oct 2006

AB [Br-77]TMC125-R165335 (etravirine) was synthesized for imaging studies by SPECT. Labelling was performed with bromine-77 by electrophilic substitution of the desbromo-precursor 4-{6-amino-2-[(4- cyanophenyl)amino]pyrimidin-4-yloxy}-3,5-dimethylbenzenecarbonitrile using carrier-free Br-77(-) and chloramine-T (CAT) as oxidizing agent. The reaction proceeded in 10 min at room temperature in aqueous DMSO as solvent. Purification was performed by HPLC, giving a chemically and radiochemically pure [Br-77]TMC125-R165335 (etravirine) in aqueous ethanol. A final radiolabelling yield of 50% is obtained.

L110 ANSWER 9 OF 13 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:221567 BIOSIS Full-text
DOCUMENT NUMBER: PREV200510005416
TITLE: Mass uniformity: Influence of operational compression conditions on breakability of scored tablets as part of manufacturing robustness evaluation.
AUTHOR(S): **De Spiegeleer, Bart** [Reprint Author]; Van Vooren, Lieven; Thonissen, Thomas; Joye, Philippe; Cornelissen, Bart; Lammens, Geert; Slegers, Guido
CORPORATE SOURCE: State Univ Ghent, Fac Pharmaceut Sci, Dept Pharmaceut Anal, Harelbekestr 72, B-9000 Ghent, Belgium
Bart.DeSpiegeleer@UGent.be
SOURCE: Journal of Food and Drug Analysis, (MAR 2005) Vol. 13, No. 1, pp. 22-29.
ISSN: 1021-9498.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Jun 2005
Last Updated on STN: 10 Jun 2005

AB Dose uniformity is a key quality element of drugs. The purpose of this study was to demonstrate a practical approach to evaluate the breakability robustness as part of the tabletting validation of a scored tablet. The influence of operational compression parameters (speed and force) on the weight variabilities of half- and quarter-tablets was investigated using two types of cross-scored round tablets of identical composition but different in size. It was shown for the used veterinary model tablet that manufacturing variation of two compression parameters around the defined target values do not significantly influence the weight variability of the broken tablets. The empirical guidance was also confirmed that for the investigated dose-proportional tablets the standard deviation of the broken tablet-part weight is linearly related to the original tablet weight. There exists a strong correlation between the variability of half-tablets and of quarter-tablets: the theoretical model previously presented was refined, demonstrating that the additional variance induced by breaking is a linear function of the break-line length. As a consequence, the standard deviation of half- and quarter-parts of cross-scored round tablets, expressed in mass units, will thus remain approximately identical. Hence, the relative standard deviation (RSD) of

quarter-tablet weights will nearly double when breaking half-tablets into quarter-tablets.

L110 ANSWER 10 OF 13 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:450181 BIOSIS Full-text
DOCUMENT NUMBER: PREV199799749384
TITLE: Effect of antibiotics on the phagocytotic and respiratory burst activity of bovine granulocytes.
AUTHOR(S): Hoeben, Dagmar [Reprint author]; **Dosogne, Hilde**; Heyneman, Roger; Burvenich, Christian
CORPORATE SOURCE: Dep. Veterinary Physiol., Biochem. Biometrics, Univ. Ghent, Fac. Veterinary Med., Salisburylaan 133, B-9820 Merelbeke, Belgium
SOURCE: European Journal of Pharmacology, (1997) Vol. 332, No. 3, pp. 289-297.
CODEN: EJPHAZ. ISSN: 0014-2999.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Oct 1997
Last Updated on STN: 27 Oct 1997

AB The influence of antibiotics on respiratory burst (phorbol-12-myristate-13-acetate (PMA)-stimulated luminol-enhanced chemiluminescence) and phagocytosis (flow cytometry) by bovine granulocytes was studied in vitro. Phagocytosis was impaired by 1000 mu-g/ml of oxytetracycline, chloramphenicol, erythromycin and spiramycin. All antibiotics, except sulphadiazine, decreased chemiluminescence at 1000 mu-g/ml or lower concentrations. Enrofloxacin increased chemiluminescence. The inhibition by oxytetracycline and danofloxacin was due to absorption of the light emitted by luminol at 425 nm. Oxytetracycline, ceftiofur, spiramycin and erythromycin affected the myeloperoxidase-H-2O-2-halide system. Ceftiofur, penicillin and danofloxacin showed scavenging effects on H-2O-2 and OCl-. Penicillin and ceftiofur might interfere with luminol. Chloramphenicol, penicillin and ceftiofur affected the production of superoxide radicals. In summary, the observed effects of antibiotics might be of importance during **treatment** of infectious diseases in normal and immunocompromised animals. However, before classifying a drug as immunosuppressive, attention has to be paid to possible interference with the chemiluminescence assay.

L110 ANSWER 11 OF 13 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-445591 [45] WPIX
DOC. NO. CPI: C2006-139301 [45]
TITLE: Oral suspension for alleviating pain and inflammation in acute/chronic musculo-skeletal disorder comprises meloxicam suspended in aqueous glycerol mixture, thickening agent, taste modifying agent and buffer system to adjust specific pH
DERWENT CLASS: A96; B02
INVENTOR: BIESMANS C P E; **DE SPIEGELEER B**
PATENT ASSIGNEE: (JANC-C) JANSSEN PHARM NV
COUNTRY COUNT: 112

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2006061351	A1	20060615	(200645)*	EN	14	[0]
NO 2007003419	A	20070703	(200753)	NO		

EP 1824493 A1 20070829 (200757) EN

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2006061351	A1	WO 2005-EP56419	20051202
NO 2007003419	A	WO 2005-EP56419	20051202
NO 2007003419	A	NO 2007-3419	20070703
EP 1824493	A1	EP 2005-850431	20051202
EP 1824493	A1	WO 2005-EP56419	20051202

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1824493	A1	Based on	WO 2006061351	A

PRIORITY APPLN. INFO: EP 2004-106318 20041206

AB WO 2006061351 A1 UPAB: 20060714

NOVELTY - A suspension (A1) comprises meloxicam (a) suspended in an aqueous glycerol mixture, a thickening agent (b), at least one taste modifying agent (c) and a buffer system (d) for maintaining a pH of 2 - 4. (A1) is free of silicon dioxide.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for preparing (A1) involving:

(A) dissolving (b) and at least one (c) in water followed by the addition of (d) to adjust the pH of 2 - 4;

(B) dissolving (a) in glycerol; and

(C) adding the aqueous mixture of step A) to the glycerol mixture of step B) while stirring to obtain a homogeneous suspension.

ACTIVITY - Analgesic; Antiinflammatory; Antiarthritic; Antirheumatic; Osteopathic; Muscular-Gen.; Dermatological.

MECHANISM OF ACTION - Cyclooxygenase-2 (COX-2) inhibitor.

USE - In the preparation of suspension; in the manufacture of a medicament for alleviating pain and inflammation in both acute and chronic musculo-skeletal disorder (claimed) in warm-blooded animals (such as dogs and cats), arthritis, rheumatoid arthritis, osteoarthritis and tenderness; for the reduction of post-operative pain and inflammation following orthopaedic and soft tissue surgery.

ADVANTAGE - The suspension is free of silicon dioxide that is no silicon dioxide is deliberately added to the instant suspension in order to achieve the stabilization; allows the use of flavoring and palatability agents that can promote animal acceptance and compliance; shows good palatability; does not have the unpleasant taste problem; effectively alleviates the disease with reduced adverse side effects; is free of caking or irreversible sedimentation of meloxicam in storage stability test; does not increase the impurities and not decrease the amount of meloxicam in storage stability test.

L110 ANSWER 12 OF 13 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-580488 [56] WPIX
DOC. NO. CPI: C2004-211535 [56]
TITLE: Composition useful in treatment of protozoal infections e.g. equine protozoal myeloencephalitis, comprises diclazuril dissolved in mixture of alcohol based solvent, emulsifier and base
DERWENT CLASS: A96; B03; C02
INVENTOR: **DE SPIEGELEER B; DOSOGNE H;** DE EPIEGELEER B

PATENT ASSIGNEE: (JANC-C) JANSSEN PHARM NV; (DSPI-I) DE SPIEGELEER B; (DOSO-I) DOSOGNE H
COUNTRY COUNT: 107

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004062673	A1	20040729	(200456)*	EN	22[0]	
EP 1587517	A1	20051026	(200570)	EN		
BR 2004006795	A	20060117	(200608)	PT		
MX 2005007601	A1	20051001	(200620)	ES		
KR 2005091062	A	20050914	(200648)	KO		
US 20060240049	A1	20061026	(200671)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004062673	A1	WO 2004-EP147	20040109
BR 2004006795	A	BR 2004-6795	20040109
EP 1587517	A1	EP 2004-701010	20040109
EP 1587517	A1	WO 2004-EP147	20040109
BR 2004006795	A	WO 2004-EP147	20040109
MX 2005007601	A1	WO 2004-EP147	20040109
KR 2005091062	A	WO 2004-EP147	20040109
KR 2005091062	A	KR 2005-712657	20050706
MX 2005007601	A1	MX 2005-7601	20050715
US 20060240049	A1	WO 2004-EP147	20040109
US 20060240049	A1	US 2005-542162	20050712

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1587517	A1	Based on	WO 2004062673	A
BR 2004006795	A	Based on	WO 2004062673	A
MX 2005007601	A1	Based on	WO 2004062673	A
KR 2005091062	A	Based on	WO 2004062673	A

PRIORITY APPLN. INFO: WO 2003-EP398 20030116
AB WO 2004062673 A1 UPAB: 20060122

NOVELTY - A composition comprises diclazuril dissolved in a mixture comprising an alcohol based solvent (A), an emulsifier (E) and a base (B) (0.5 - 3 mol equivalents).

ACTIVITY - Protozoacide; Antiparasitic.

MECHANISM OF ACTION - None given.

USE - In the treatment of protozoal infections e.g. Equine Protozoal Myeloencephalitis (claimed) and coccidiose; for treatment of parasitic protozoa.

ADVANTAGE - The composition avoid the use of solvents with a relatively high toxic profile such as dimethylsulfoxide, dimethylformamide or tetrahydrofuran which upon dilution with aqueous systems can cause precipitation of the active drug substance. The solvent systems have good bioavailability and can be tailored for oral, transdermal or parenteral administration. The composition is stable upon dilution with aqueous system such as artificial gastric fluid and artificial intestinal fluid. (A) Has low toxicity and is resistant to precipitation upon dilution with aqueous system thus reduces the risk of low and variable bioavailability as well as local irritation after parenteral administration. Effective plasma concentration can

be attained within a short time period after administration of the composition leading to rapid entry of diclazuril into infected tissue thus the period of treatment is shorter. Smaller quantities of diclazuril were required thus the cost of drug is less. The composition is stable below 25 degrees C and the amount of keto-degradation products of diclazuril can be maintained below 3 %.

L110 ANSWER 13 OF 13 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-037441 [04] WPIX
DOC. NO. CPI: C2004-014921 [04]
TITLE: Broad spectrum veterinary antiparasitic composition comprising macrocyclic lactone, e.g. ivermectin, and closantel, in oily vehicle
DERWENT CLASS: B02; C02
INVENTOR: **DE SPIEGELEER B**; DELHOM N; DERRIEU G
PATENT ASSIGNEE: (JANC-C) JANSSEN PHARM NV; (VIRB-N) VIRBAC SA
COUNTRY COUNT: 102

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
FR 2839614	A1	20031121	(200404)*	FR	26	[4]
WO 2003099259	A1	20031204	(200406)	FR		
AU 2003258756	A1	20031212	(200443)	EN		
EP 1503733	A1	20050209	(200512)	FR		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
FR 2839614	A1	FR 2002-5899	20020514
AU 2003258756	A1	AU 2003-258756	20030512
EP 1503733	A1	EP 2003-755163	20030512
WO 2003099259	A1	WO 2003-FR1432	20030512
EP 1503733	A1	WO 2003-FR1432	20030512

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2003258756	A1	Based on	WO 2003099259 A
EP 1503733	A1	Based on	WO 2003099259 A

PRIORITY APPLN. INFO: FR 2002-5899 20020514
AB FR 2839614 A1 UPAB: 20050906
NOVELTY - An oily composition (I) comprises:
(a) an oil vehicle;
(b) at least one macrocyclic lactone dissolved in (a); and
(c) at least one of closantel and its salts suspended in (a).
ACTIVITY - Anthelmintic; Antiparasitic.
MECHANISM OF ACTION - None given in the source material.
USE - (I) Is useful in the production of a medicament for the prevention and/or treatment of infections by endoparasites or ectoparasites, especially plathelminths, nemathelminths or arthropods. (I) Is especially useful for veterinary use, particularly in livestock or pets.
ADVANTAGE - (I) Is effective at relatively low doses against a broad spectrum of parasites (e.g. Fasciola hepatica. Haemonchus contortus, Chabertia ovina and Hypoderma larvae), shows good bioavailability and high physical and chemical stability, is easy to administer orally to animals, and is non-toxic

to the animals, personnel administering the composition and the environment. The stability of the active agents (b) and (c) over 2 years is at least 90% (especially at least 95%) (claimed).

******* QUERY RESULTS *******

```
=> d his l62

     (FILE 'HCAPLUS' ENTERED AT 10:07:26 ON 31 OCT 2007)
L62            4 S L45 OR L61

=> d que l62
L2             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  DICLAZURIL/CN
L3             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  101831-37-2
L4             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 OR L3
L5             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ETHANOL/CN
L6             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  64-17-5/RN
L7             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 OR L6
L8             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SODIUM HYDROXIDE/CN
L9             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  64-17-5/RN
L10            2 SEA FILE=REGISTRY ABB=ON  PLU=ON  L8 OR L9
L11            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ETHANOLAMINE/CN
L12            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  141-43-5 /RN
L13            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L11 OR L12
L16            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  N-METHYLGLUCAMINE/CN
L17            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  6284-40-8/RN
L18            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L16 OR L17
L20          143 SEA FILE=HCAPLUS ABB=ON   PLU=ON  DICLAZURIL/BI
L21          154 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L20 OR L4
L22       284893 SEA FILE=HCAPLUS ABB=ON   PLU=ON  ETHANOL/BI
L23       332305 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L22 OR L7
L24         2847 SEA FILE=HCAPLUS ABB=ON   PLU=ON  (PEG(W)400 OR PEG400 OR
                 PEG-400 OR POLYETHYLENEGLYCOL(W)400)/BI
L29          509 SEA FILE=HCAPLUS ABB=ON   PLU=ON  N/OBI(W)METHYLGLUCAMINE/BI
L30        99844 SEA FILE=HCAPLUS ABB=ON   PLU=ON  SODIUM HYDROXIDE/BI
L31        26353 SEA FILE=HCAPLUS ABB=ON   PLU=ON  ETHANOLAMINE/BI
L33         1528 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L29 OR L18
L34       325195 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L10 OR L30
L35        41162 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L13 OR L31
L36          701 SEA FILE=HCAPLUS ABB=ON   PLU=ON  ANTI/OBI(W)PROTOZOAL?/OBI OR
                 ANTIPROTOZOAL?/OBI
L37         4809 SEA FILE=HCAPLUS ABB=ON   PLU=ON  (PROTOZOAL/OBI OR CENTRAL
                 NERVOUS SYSTEM?/OBI OR CNS/OBI OR CEREBRAL PROTOZOAL/OBI) (W)
                 (INFECT?/OBI OR DISEASE?/OBI)
L38          210 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L36 (L) (AGENT?/OBI)
L39            9 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L21 AND (L36 OR L37 OR L38)
L40           11 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L21 AND (L23 OR L24)
L43           10 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L21 AND (L33 OR L34 OR L35)
L45            3 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L39 (L) (L40 OR L43)
L47         4034 SEA FILE=HCAPLUS ABB=ON   PLU=ON  PROTOZOACIDE?/BI
L49       156714 SEA FILE=HCAPLUS ABB=ON   PLU=ON  ALCOHOLS/CT
L50        29739 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L49 (L) (THU OR BIOL)/RL
L51        60391 SEA FILE=HCAPLUS ABB=ON   PLU=ON  SOLVENTS/CT
L55           46 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L47 AND L50
L56            7 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L55 AND L51
L58        45011 SEA FILE=HCAPLUS ABB=ON   PLU=ON  EMULSIFIER?/BI
L59            2 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L56 AND L58
L60            1 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L56 AND (L36 OR L37)
L61            2 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L59 OR L60
L62            4 SEA FILE=HCAPLUS ABB=ON   PLU=ON  L45 OR L61


=> d his l73
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     (FILE 'WPIX' ENTERED AT 10:35:50 ON 31 OCT 2007)
L73            2 S L72 AND (L22 OR PEG()400 OR PEG400 OR PEG-400 OR POLYETHYLENE

=> d que l73
L2             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  DICLAZURIL/CN
L3             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  101831-37-2
L4             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L2 OR L3
L20          143 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DICLAZURIL/BI
L22       284893 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ETHANOL/BI
L36          701 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTI/OBI(W)PROTOZOAL?/OBI OR
                 ANTIPROTOZOAL?/OBI
L37         4809 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (PROTOZOAL/OBI OR CENTRAL
                 NERVOUS SYSTEM?/OBI OR CNS/OBI OR CEREBRAL PROTOZOAL/OBI) (W)
                 (INFECT?/OBI OR DISEASE?/OBI)
L71           30 SEA FILE=WPIX ABB=ON  PLU=ON  L20 OR L4
L72           11 SEA FILE=WPIX ABB=ON  PLU=ON  L71 AND (L36 OR L37)
L73            2 SEA FILE=WPIX ABB=ON  PLU=ON  L72 AND (L22 OR PEG(W)400 OR
                 PEG400 OR PEG-400 OR POLYETHYLENEGLYCOL(W)400 OR N-METHYLGLUCAM
                 INE OR SODIUM HYDRIDE OR ETHANOLAMINE OR TRIETHANYLAMINE)


=> dup rem l62 l73
PROCESSING COMPLETED FOR L62
PROCESSING COMPLETED FOR L73
L111           5 DUP REM L62 L73 (1 DUPLICATE REMOVED)
                 ANSWERS '1-4' FROM FILE HCAPLUS
                 ANSWER '5' FROM FILE WPIX

=> d l111 1-4 ibib ed abs hitind; d l111 5 iall abeq tech abex

L111 ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2004:610087  HCAPLUS  Full-text
DOCUMENT NUMBER:          141:145721
TITLE:                    Anti-protozoal compositions
                          comprising diclazuril
INVENTOR(S):              De Spiegeleer, Bart; Dosogne, Hilde
PATENT ASSIGNEE(S):       Janssen Pharmaceutica N.V., Belg.
SOURCE:                   PCT Int. Appl., 22 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    ---------------------    --------
     WO 2004062673         A1    20040729    WO 2004-EP147            20040109
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ
     CA 2512176            A1    20040729    CA 2004-2512176          20040109
     EP 1587517            A1    20051026    EP 2004-701010           20040109
     EP 1587517            B1    20071024
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     BR 2004006795         A     20060117    BR 2004-6795             20040109
     US 2006240049         A1    20061026    US 2005-542162           20050712
     MX 2005PA07601        A     20050930    MX 2005-PA7601           20050715
PRIORITY APPLN. INFO.:                       WO 2003-EP398       A    20030116
```

WO 2003-EP300398 A 20030116
WO 2004-EP147 W 20040109

ED Entered STN: 30 Jul 2004

AB The present invention relates to compns. suitable for oral, transdermal or parenteral (e.g. intranasal, i.m., s.c. or i.v.) administration, wherein the composition is comprised of at least one anti-protozoal agent dissolved in a mixture of an alc. based solvent-system, an **emulsifier**-system and a base-system. Also provided is a method for preparing said anti-protozoal compns. and their use in the treatment or prevention of protozoal infections in warm-blooded animals, including humans.

IC ICM A61K031-53
ICS A61K047-10; A61K047-18; A61K047-32; A61K009-08; A61P033-02

CC 63-6 (Pharmaceuticals)

ST **diclazuril protozoacide** formulation

IT Drug bioavailability
Emulsifying **agents**
Protozoacides
Solvents
(**anti-protozoal** compns. comprising **diclazuril**)

IT Glycols, biological studies
Polyoxyalkylenes, biological studies
Sterols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**anti-protozoal** compns. comprising **diclazuril**)

IT Encephalomyelitis
(equine protozoal; **anti-protozoal** compns. comprising **diclazuril**)

IT Castor oil
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ethoxylated; **anti-protozoal** compns. comprising **diclazuril**)

IT **Alcohols, biological studies**
RL: **THU (Therapeutic use); BIOL (Biological study);** USES (Uses)
(fatty; **anti-protozoal** compns. comprising **diclazuril**)

IT Surfactants
(ionic; **anti-protozoal** compns. comprising **diclazuril**)

IT Drug delivery systems
(oral; **anti-protozoal** compns. comprising **diclazuril**)

IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyethoxylated; **anti-protozoal** compns. comprising **diclazuril**)

IT **Alcohols, biological studies**
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); **THU (Therapeutic use); BIOL (Biological study)**; PROC (Process); USES (Uses)
(polyhydric; **anti-protozoal** compns. comprising **diclazuril**)

IT **101831-37-2, Diclazuril**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**anti-protozoal** compns. comprising

diclazuril)
IT 106392-12-5
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-protozoal compns. comprising diclazuril)
IT 74-89-5, Methylamine, uses 75-04-7, Ethylamine, uses 75-50-3, Trimethylamine, uses 107-15-3, Ethylenediamine, uses 109-89-7, Diethylamine, uses 121-44-8, Triethylamine, uses 124-40-3, Dimethylamine, uses **141-43-5, Ethanolamine**, uses 144-55-8, Sodium bicarbonate, uses 298-14-6, Potassium bicarbonate 497-19-8, Sodium carbonate, uses 506-87-6, Ammonium carbonate 584-08-7, Potassium carbonate 631-61-8, Ammonium acetate 1305-62-0, Calcium hydroxide, uses 1309-42-8, Magnesium hydroxide 1310-58-3, Potassium hydroxide, uses 1310-65-2, Lithium hydroxide **1310-73-2, Sodium hydroxide**, uses **6284-40-8, N-Methylglucamine**
RL: NUU (Other use, unclassified); USES (Uses)
(anti-protozoal compns. comprising diclazuril)
IT 57-55-6D, Propylene glycol, esters 12441-09-7D, Sorbitan, derivs. 25322-68-3, Polyethyleneglycol 112209-99-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-protozoal compns. comprising diclazuril)

L111 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:409695 HCAPLUS Full-text
DOCUMENT NUMBER: 144:440098
TITLE: Methods and formulations for enhancing the absorption and gastro-intestinal bioavailability of hydrophobic drugs
INVENTOR(S): Spilburg, Curtis A.
PATENT ASSIGNEE(S): Kapac, LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 7 pp., Cont.-in-part of U.S. Ser. No. 149,862.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006093661	A1	20060504	US 2005-291126	20051130
US 2003212046	A1	20031113	US 2002-140620	20020507
US 2005244488	A1	20051103	US 2005-149862	20050610
PRIORITY APPLN. INFO.:			US 2002-140620	A2 20020507
			US 2005-149862	A2 20050610

ED Entered STN: 05 May 2006
AB The present invention relates to a general method and delivery composition for enhancing the bioavailability of hydrophobic, poorly water soluble compound and gastro-intestinal drugs. The hydrophobic drug delivery system includes a plant derived sterol (stanol) or a sterol (stanol) derived ester, an **emulsifier** and an active, hydrophobic drug, all dissolved and then dried to form a liposome delivery system.
INCL 424450000; 435458000
CC 63-6 (Pharmaceuticals)
IT **Alcohols, biological studies**
RL: **THU (Therapeutic use); BIOL (Biological study);**

USES (Uses)
(fatty; methods and formulations for enhancing absorption and gastro-intestinal bioavailability of hydrophobic drugs)

IT Anesthetics
Antiasthmatics
Antibiotics
Anticonvulsants
Antidepressants
Antidiabetic agents
Antiobesity agents
Antipsychotics
Antipyretics
Antitumor agents
Antiviral agents
Cardiovascular agents
Dietary supplements
Diuretics
Egg, poultry
Emulsifying agents
Food
Fungicides
Gastrointestinal agents
Glycine max
Immunosuppressants
Muscle relaxants
Nervous system stimulants
Protozoacides
(methods and formulations for enhancing absorption and gastro-intestinal bioavailability of hydrophobic drugs)

IT **Solvents**
(organic, non-polar; methods and formulations for enhancing absorption and gastro-intestinal bioavailability of hydrophobic drugs)

L111 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:775892 HCAPLUS Full-text
DOCUMENT NUMBER: 141:296019
TITLE: **Antiprotozoal** imidazopyridine compounds and their preparation, use, and compositions for the treatment of coccidiosis in poultry or **protozoal diseases** in mammals
INVENTOR(S): Wyvratt, Matthew J.; Biftu, Tesfaye; Fisher, Michael H.; Schmatz, Dennis M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080390	A2	20040923	WO 2004-US6153	20040302
WO 2004080390	A3	20050120		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004220648	A1	20040923	AU 2004-220648	20040302
CA 2517427	A1	20040923	CA 2004-2517427	20040302
EP 1603900	A2	20051214	EP 2004-716431	20040302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
JP 2006520819	T	20060914	JP 2006-508940	20040302
US 2006178358	A1	20060810	US 2005-548154	20050906
PRIORITY APPLN. INFO.:			US 2003-452467P	P 20030306
			WO 2004-US6153	A 20040302

OTHER SOURCE(S): MARPAT 141:296019
ED Entered STN: 23 Sep 2004
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compds. described by I and their pharmaceutically acceptable salts and/or N-oxides are disclosed [wherein: R1 = H, Me, or F; R2 = H or Me; R3 = -L-NRcRd, or various mono- and bicyclic saturated amines bound at carbon, e.g., piperidin-4-yl; L = (CRaRb)2-5 or C3-5 cycloalkane-1,1-diyl; Ra, Rb = H, OH, F, or C1-4 alkyl, provided that when Ra = OH, the vicinal Rb is H or C1-4-alkyl; or RaRb forms C3-6 cycloalkyl; Rc, Rd = H or C1-4 alkyl; n, m = 0-4, provided that (n+m) = 2, 3, or 4]. The compds. are useful (no data) for the treatment and prevention of protozoal diseases in mammals and birds. A method for controlling coccidiosis in poultry comprises administering an effective amount of I alone, or in combination with one or more anticoccidial agent(s). A composition for controlling coccidiosis in poultry comprises the compound alone, or in combination with one or more anticoccidial agent(s). Methods for the treatment and prevention of mammalian protozoal diseases, such as, for example, toxoplasmosis, malaria, African trypanosomiasis (sleeping sickness), Chagas' disease, and opportunistic infections, comprise administering I alone, or in combination with one or more other antiprotozoal agent(s). For instance, invention compound II was prepared in 10 steps from 2-mercapto-4-methylpyrimidine hydrochloride: (1) S-methylation (91%), (2) lithiation of the 4-Me group and α-aroylation with Me 4-fluorobenzoate (43%), (3) α-bromination of the formed ketone (100%), (4) cyclocondensation of the α-bromo ketone with 2-amino-4-(hydroxymethyl)pyridine to give (43%) intermediate III, (5) O-mesylation of the alc. in III (85%), (6) cyanation of the mesylate with NBu4CN (67%), (7) oxidation of the methylthio group to a sulfone (91%), (8) hydrogenation of the cyanomethyl sidechain to give aminoethyl (>100% crude), (9) ammonolysis of the sulfone to give an amino group (26% over 2 steps), and finally (10) N,N-dimethylation with formaldehyde and NaBH3CN in the presence of AcOH. Seven synthetic examples and four prophetic examples are given. Twelve compds. I are individually claimed. Combined anticoccidial use of I in poultry with a variety of named coccidiostats is also claimed.

IC ICM A61K

CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 18, 63

ST imidazopyridine **antiprotozoal** prepn treatment coccidiosis malaria trypanosomiasis toxoplasmosis Chagas; protozoacide imidazopyridine prepn anticoccidial poultry feed antimalarial trypanosomicide

IT Infection
(Chagas' disease, treatment of; preparation of **antiprotozoal**

imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

IT Feed additives
(compds. for; preparation of **antiprotozoal** imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

IT Infection
(opportunistic, treatment of; preparation of **antiprotozoal** imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

IT Feed
(poultry, compds. for; preparation of **antiprotozoal** imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

IT Antimalarials
Combination chemotherapy
Protozoacides
Trypanosomicides
(preparation of **antiprotozoal** imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

IT Infection
(toxoplasmosis, treatment of; preparation of **antiprotozoal** imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

IT Poultry
(treatment of coccidiosis in; preparation of **antiprotozoal** imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

IT Protozoa
(treatment of infection; preparation of **antiprotozoal** imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

IT Coccidiosis
Malaria
(treatment of; preparation of **antiprotozoal** imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

IT Infection
(trypanosomiasis, treatment of; preparation of **antiprotozoal** imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

IT 57-62-5 59-06-3, Ethopabate 79-57-2, Oxytetracycline 121-25-5, Amprolium 148-01-6, Dinitolmide 330-95-0, Nicarbazin 2971-90-6, Clopidol 11054-70-9, Lasalocid 17090-79-8, Monensin 18507-89-6, Decoquinate 25875-51-8, Robenidine 53003-10-4, Salinomycin 55134-13-9, Narasin 55837-20-2, Halofuginone **101831-37-2**, **Diclazuril** 113378-31-7, Semduramicin 119758-39-3, Maduramicin
RL: AGR (Agricultural use); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coccidiostatic compns. also containing; preparation of **antiprotozoal** imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

IT 762172-76-9P, 4-[7-(2-Aminoethyl)-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-yl]pyrimidin-2-amine 762172-78-1P, 4-[7-(2-Amino-1,1-dimethylethyl)-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-yl]pyrimidin-2-amine 762172-80-5P, 4-[2-(4-Fluorophenyl)-7-(piperidin-4-yl)imidazo[1,2-a]pyridin-3-yl]pyrimidin-2-amine
RL: AGR (Agricultural use); FFD (Food or feed use); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic

use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of **antiprotozoal** imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

IT 762172-77-0P, 4-[7-[2-(Dimethylamino)ethyl]-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-yl]pyrimidin-2-amine 762172-79-2P, 4-[7-[2-(Dimethylamino)-1,1-dimethylethyl]-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-yl]pyrimidin-2-amine 762172-81-6P, 4-[2-(4-Fluorophenyl)-7-(1-methylpiperidin-4-yl)imidazo[1,2-a]pyridin-3-yl]pyrimidin-2-amine 762172-82-7P, 1-[3-(2-Aminopyrimidin-4-yl)-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-7-yl]-2-(dimethylamino)**ethanol** 762172-83-8P, 4-[2-(4-Fluorophenyl)-7-(1-ethylpiperidin-4-yl)imidazo[1,2-a]pyridin-3-yl]pyrimidin-2-amine 762172-84-9P, 4-[2-(4-Fluorophenyl)-7-(1-azabicyclo[2.2.2]oct-4-yl)imidazo[1,2-a]pyridin-3-yl]pyrimidin-2-amine 762172-85-0P, 4-[2-(4-Fluorophenyl)-7-(1-methylazetidin-3-yl)imidazo[1,2-a]pyridin-3-yl]pyrimidin-2-amine 762172-86-1P, 4-[2-(4-Fluorophenyl)-7-(1-methylpyrrolidin-3-yl)imidazo[1,2-a]pyridin-3-yl]pyrimidin-2-amine 762172-87-2P, 4-[7-[2-(Dimethylamino)-2-methylpropyl]-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-yl]pyrimidin-2-amine 762172-88-3P, 4-[7-[2-(Dimethylamino)-1-methylethyl]-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-yl]pyrimidin-2-amine 762172-89-4P, 4-[7-[3-(Dimethylamino)propyl]-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-3-yl]pyrimidin-2-amine 762172-90-7P, 4-[2-(4-Fluorophenyl)-7-[(1-methylazetidin-2-yl)methyl]imidazo[1,2-a]pyridin-3-yl]pyrimidin-2-amine
RL: AGR (Agricultural use); FFD (Food or feed use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of **antiprotozoal** imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

IT 14001-63-9P, 4-Methyl-2-(methylthio)pyrimidine 31251-23-7P, Benzyl 4-(pyridin-4-yl)piperidine-1-carboxylate 217661-99-9P, 2-[2-(Methylthio)pyrimidin-4-yl]-1-(4-fluorophenyl)ethanone 266358-16-1P, 2-Bromo-2-[2-(methylthio)pyrimidin-4-yl]-1-(4-fluorophenyl)ethanone 480453-78-9P, [2-(4-Fluorophenyl)-3-[2-(methylthio)pyrimidin-4-yl]imidazo[1,2-a]pyridin-7-yl]methanol 762172-91-8P, 2-[2-(Methylthio)pyrimidin-4-yl]-1-(4-fluorophenyl)ethen-1-ol 762172-92-9P, [2-(4-Fluorophenyl)-3-[2-(methylthio)pyrimidin-4-yl]imidazo[1,2-a]pyridin-7-yl][(methanesulfonyl)oxy]methane 762172-93-0P, [2-(4-Fluorophenyl)-3-[2-(methylthio)pyrimidin-4-yl]imidazo[1,2-a]pyridin-7-yl]acetonitrile 762172-94-1P, [2-(4-Fluorophenyl)-3-[2-(methanesulfonyl)pyrimidin-4-yl]imidazo[1,2-a]pyridin-7-yl]acetonitrile 762172-95-2P, 2-[2-(4-Fluorophenyl)-3-[2-(methanesulfonyl)pyrimidin-4-yl]imidazo[1,2-a]pyridin-7-yl]ethanamine 762172-96-3P, 2-[2-(4-Fluorophenyl)-3-[(2-methylsulfanyl)pyrimidin-4-yl]imidazo[1,2-a]pyridin-7-yl]-2-methylpropanenitrile 762172-97-4P, 2-[2-(4-Fluorophenyl)-3-[2-(methylsulfonyl)pyrimidin-4-yl]imidazo[1,2-a]pyridin-7-yl]-2-methylpropanenitrile 762172-98-5P, 2-[3-(2-Aminopyrimidin-4-yl)-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-7-yl]-2-methylpropanenitrile 762172-99-6P, 2-Bromo-1-(4-fluorophenyl)ethanone O-methyloxime 762173-00-2P, Benzyl 4-[2-(4-fluorophenyl)imidazo[1,2-a]pyridin-7-yl]piperidine-1-carboxylate 762173-01-3P, Benzyl 4-[3-acetyl-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-7-yl]piperidine-1-carboxylate 762173-02-4P, Benzyl 4-[3-(2-aminopyrimidin-4-yl)-2-(4-fluorophenyl)imidazo[1,2-a]pyridin-7-yl]piperidine-1-carboxylate 762173-03-5P, 2-(4-Fluorophenyl)-3-[2-(methylthio)pyrimidin-4-yl]imidazo[1,2-a]pyridine-7-carboxaldehyde 762173-04-6P, 2-(4-Fluorophenyl)-7-(3-methyl-1,3-oxazolidin-5-yl)-3-[2-(methylthio)pyrimidin-4-yl]imidazo[1,2-a]pyridine 762173-05-7P,

1-[2-(4-Fluorophenyl)-3-[2-(methylthio)pyrimidin-4-yl]imidazo[1,2-a]pyridin-7-yl]-2-(dimethylamino)**ethanol** 762173-06-8P, 1-[2-(4-Fluorophenyl)-3-[2-(methylsulfonyl)pyrimidin-4-yl]imidazo[1,2-a]pyridin-7-yl]-2-(dimethylamino)**ethanol**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of **antiprotozoal** imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

IT 107-97-1, Sarcosine 403-29-2, 4-Fluorophenacyl bromide 403-33-8, Methyl 4-fluorobenzoate 581-45-3, 4-(Piperidin-4-yl)pyridine 6959-66-6, 2-Mercapto-4-methylpyrimidine hydrochloride 105250-17-7, 2-Amino-4-(hydroxymethyl)pyridine
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of **antiprotozoal** imidazopyridines for treatment of coccidiosis in poultry or **protozoal diseases** in mammals)

L111 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:240901 HCAPLUS Full-text
DOCUMENT NUMBER: 132:270082
TITLE: Novel compositions and methods for prevention and treatment of **protozoal disease**
INVENTOR(S): Hundley, Bruce; Maclin, Robert; Delucca, Patrick; Gebrekidan, Sisay
PATENT ASSIGNEE(S): New Ace Research Co., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000019964	A2	20000413	WO 1999-US23566	19991008
WO 2000019964	A3	20000914		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2346463	A1	20000413	CA 1999-2346463	19991008
BR 9914385	A	20010717	BR 1999-14385	19991008
EP 1119255	A2	20010801	EP 1999-950279	19991008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 510998	A	20030228	NZ 1999-510998	19991008
AU 766542	B2	20031016	AU 1999-62972	19991008
WO 2001026660	A1	20010419	WO 2000-US8110	20000327
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,				

CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

ZA 2001002871	A	20020806	ZA 2001-2871		20010406
MX 2001PA03542	A	20020918	MX 2001-PA3542		20010406
IN 2001KN00402	A	20050311	IN 2001-KN402		20010409
US 6465460	B1	20021015	US 2001-806975		20010913
HK 1043019	A1	20050513	HK 2002-104593		20020620
US 2003096815	A1	20030522	US 2002-233868		20020903
PRIORITY APPLN. INFO.:			US 1998-103543P	P	19981008
			US 1998-112175P	P	19981214
			WO 1999-US23566	W	19991008
			US 2001-806975	A1	20010913

ED Entered STN: 14 Apr 2000

AB A composition is provided that has been specially adapted for parenteral administration, e.g., intranasal, i.m., s.c., transdermal or i.v. administration, wherein the composition is comprised of at least one anti-protozoal drug in a therapeutically effective amount for the treatment or prevention of protozoan infections in man and in animals. In one embodiment, the anti-protozoal drug is a triazine-based anticoccidial agent, e.g., a triazinedione or triazinetrione such as **diclazuril** , toltrazuril, sulfonotoltrazuril or water-soluble sodium salts thereof. In a presently preferred embodiment, the triazine-based anticoccidial agent is sulfonotoltrazuril. Methods of treatment of protozoal infections in man and animals are also provided. Blood concentration following single i.v. administration of 750 mg **diclazuril** and repeated i.v. administration of 0.5mg/lb once a day in horses was studied.

ICI A61

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

ST **antiprotozoal** drug protozoan disease

IT Babesia
Cryptosporidium
(infection with; novel compns. and methods for prevention and treatment of **protozoal disease**)

IT Drug delivery systems
(injections, i.v.; novel compns. and methods for prevention and treatment of **protozoal disease**)

IT Drug delivery systems
(injections, s.c.; novel compns. and methods for prevention and treatment of **protozoal disease**)

IT Drug delivery systems
(nasal; novel compns. and methods for prevention and treatment of **protozoal disease**)

IT Anti-inflammatory agents
(nonsteroidal; novel compns. and methods for prevention and treatment of **protozoal disease**)

IT Coccidiostats
Drug bioavailability
Encephalomyelitis
Protozoacides
(novel compns. and methods for prevention and treatment of **protozoal disease**)

IT Sulfonamides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel compns. and methods for prevention and treatment of **protozoal disease**)

IT Drug delivery systems
(oral; novel compns. and methods for prevention and treatment of **protozoal disease**)

IT Solvents
(organic; novel compns. and methods for prevention and treatment of **protozoal disease**)
IT Drug delivery systems
(parenterals; novel compns. and methods for prevention and treatment of **protozoal disease**)
IT Infection
(protozoal; novel compns. and methods for prevention and treatment of **protozoal disease**)
IT Drug delivery systems
(transdermal; novel compns. and methods for prevention and treatment of **protozoal disease**)
IT 112209-99-1P, Sodium **diclazuril**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel compns. and methods for prevention and treatment of **protozoal disease**)
IT 58-14-0, Pyrimethamine 55981-09-4, Nitazoxanide 69004-03-1, Toltrazuril 69004-04-2 101831-36-1, Clazuril **101831-37-2**, **Diclazuril** 103337-74-2, Letrazuril
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel compns. and methods for prevention and treatment of **protozoal disease**)
IT 67-68-5, Dmso, uses 127-19-5, Dma
RL: NUU (Other use, unclassified); USES (Uses)
(novel compns. and methods for prevention and treatment of **protozoal disease**)
IT **1310-73-2**, **Sodium hydroxide**, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(novel compns. and methods for prevention and treatment of **protozoal disease**)

L111 ANSWER 5 OF 5 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-417621 [44] WPIX
DOC. NO. CPI: C2001-126153 [44]
TITLE: New 2-aryl-5-(4-piperidyl)-3-(4-pyridyl)-pyrrole derivatives, useful for treating **protozoal infections** including coccidiosis in poultry
DERWENT CLASS: B02; B03; C02
INVENTOR: BIFTU T; FENG D D; FISCHER M H; FISHER M H; GIROTRA N; LIANG G; PONPIPOM M M; QIAN X; WYVRATT M J
PATENT ASSIGNEE: (MERI-C) MERCK & CO INC
COUNTRY COUNT: 91

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001034150	A1	20010517	(200144)*	EN	64[0]	
AU 2001015961	A	20010606	(200152)	EN		
US 6432980	B1	20020813	(200255)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001034150 A1		WO 2000-US30948	20001110
US 6432980 B1	Provisional	US 1999-165143P	19991112
US 6432980 B1		US 2000-710165	20001110
AU 2001015961 A		AU 2001-15961	20001110

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001015961 A	Based on	WO 2001034150 A

PRIORITY APPLN. INFO: US 1999-165143P 19991112
US 2000-710165 20001110
INT. PATENT CLASSIF.:
IPC RECLASSIF.: A61K0031-4523 [I,C]; A61K0031-4545 [I,A]; C07D0401-00 [I,C]; C07D0401-14 [I,A]; C07D0413-00 [I,C]; C07D0413-14 [I,A]

BASIC ABSTRACT:

WO 2001034150 A1 UPAB: 20050901

NOVELTY - 2-Aryl-5-(4-piperidyl)-3-(4-pyridyl)-pyrrole derivatives (I) and their salts are new.

DETAILED DESCRIPTION - 2-Aryl-5-(4-piperidyl)-3-(4-pyridyl)- pyrrole derivatives of formula (I) and their salts are new.

n = 0 or 1;

p = 1-3;

R = halo;

R1 = H or 1-6C alkyl;

X = a bond or alkylidene;

R2, R3 = optionally substituted hydrocarbyl, carboxylate derivative or oxo;

R4 = amino derivative;

R5, R6 = H or hydrocarbyl derivative; and

R7 = O or Me.

INDEPENDENT CLAIMS are included for (i)

(1) a method for treating **protozoal diseases** comprising administration of (I);

(2) a method of treating coccidiosis in poultry comprising administration of (I); (iii) compositions comprising (I)

ACTIVITY - Protozoacide

MECHANISM OF ACTION - None given.

USE - (I) are useful for treating **protozoal diseases** (e.g. amoebiasis, giardiasis, malaria, leishmaniasis, trypanosomiasis, toxoplasmosis, babesiosis, cryptosporidiosis, dysentery, vaginitis, coccidiosis and enterohepatitis), especially coccidiosis in poultry.

MANUAL CODE: CPI: B02-Z; B06-H; B07-H; B10-A13D; B10-A17; B10-D03; B14-A03; B14-A03C; C02-Z; C06-H; C07-H; C10-A13D; C10-A17; C10-D03; C14-A03; C14-A03C

TECH

ORGANIC CHEMISTRY - Preparation: An example for the preparation of (I) comprises reacting a substituted pyrrole of formula (II) with an alkyl halide of formula (III) in the presence of a strong base e.g. **sodium hydride** and in a solvent e.g dimethylformamide.

L = Br, Cl or preferably I.

ABEX DEFINITIONS - Full Definitions: - n = 0 or 1; - p = 1-3; - X = a bond, (CRaRa)p, 3-7C cycloalkylene or 3-7C cycloalkylidene; - R = halo; - R1 = H or 1-6C alkyl; - R2, R3 = H, 1-6C alkyl (optionally substituted by ORb), 2-6C alkenyl, 2-6C alkynyl, phenyl (optionally substituted by ORb), benzyl (optionally substituted by ORb) or COORb; - R2+R3 = =O or when X = a bond

or (CRaRa)p; or - R2+R4 = 4- to 7-membered non-aromatic ring (containing NRf and optionally substituted by 1-3 of =O or Rd); or - R2+R5 = 4- to 7-membered non-aromatic ring (containing up to 2 heteroatoms (NRf, O or SOm) and optionally substituted by 1-5 of =O, ORb, CH2ORb or 1-6C alkyl); - m = 0-2; - R4 = NRbRb, NRbCORb, NRbCOORb, NRbCONRbRb, NRbSO2Rb, NRbC(=NRb)NRbRb or CONRbRb; or - R4-C-R5 = 3- to 7-membered non-aromatic ring (containing NRf and optionally containing an additional heteroatom (O, SOm or NRf) and optionally substituted by up to 3 of =O or Rd); - R5, R6 = H, 1-12C alkyl, 2-12C alkenyl, 2-12C alkynyl, 3-7C cycloalkyl-(1-6C alkyl)n, heterocyclyl-(1-6C alkyl)n, aryl-(1-6C alkyl)n or heteroaryl-(1-6C alkyl)n in which the alkyl, alkenyl and alkynyl are optionally substituted by 1-5 of Rc and the cycloalkyl, heterocyclyl, aryl or heteroaryl are optionally substituted by 1-3 of Rd; or - R5-C-R6 = 3- to 7-membered non-aromatic carbocyclic ring (optionally substituted by up to 3 of =O or Rd); or - R5+R6 = =O or - R5+Ra = 3- to 7-membered non-aromatic carbocyclic ring when X = (CRaRa)p; - R7 = O or Me; - Ra = H, 1-6C alkyl or ORb; - Rb = R5 or ; - Rb-N-Rb = 3- to 7-membered optionally unsaturated or aromatic ring (optionally containing an additional heteroatom (O, SOm, N or NRf), optionally benzo-fused and optionally substituted by 1-3 of =O or Rd) - Rc = NReRe, NRgCOORe, NRgCORe, NRgCONReRe, NRgSO2Re, halo, SOmRe, ORe, OCONReRe, OCOORe, OCORe, OSO2Re, OCF3, CF3, COORe, CORe, =O, N3, CN, NO2 or P(O)(ORe)2; - Rd = 1-6C alkyl (optionally substituted by 1-5 of Rc), Rc, aryl (optionally substituted by 1-5 of Rc) or heteroaryl (optionally substituted by 1-5 of Rc); - Re = H, 1-12C alkyl, 2-12C alkenyl, 2-12C alkynyl, 3-7C cycloalkyl-(1-6C alkyl)n, aryl-(1-6C alkyl)n or heteroaryl-(1-6C alkyl)n all optionally substituted by 1-2 of OH or 1-3C alkoxy; or ; - Re-N-Re = 3- to 7-membered ring (optionally containing and additional heteroatom (O, S or NRg)) - Rf = Re, CORe, COORe, CONReRe or SO2Re; and - Rg = H, 1-6C alkyl or aryl-(1-6C alkyl) provided that when R4 = NH2 or tert-butoxycarbonylamino, R1 = R5 = R6 = H and X = a bond then R2+R3 is not =O. - Preferred Definitions: - R = 4-F; - R1, R3 = H; - R7 = absent; and - X = CH(OH) or a bond.

ADMINISTRATION - The dose of (I) is 1-1000 mg/kg preferably parenterally, orally, topically or rectally or for poultry in foodstuff. (I) may also be administered with another anticoccoidial agent, especially amprolium, ethopabate, clopidol, meticlorpindol, decoquinate, dinitolamide, halofuginone, lasalocid, maduramicin, monensin, narasin, nicarbazin, chlortetracycline, oxytetracycline, robenidine, salinomycin, semduramicin or diclazuril.

SPECIFIC COMPOUNDS - 164 specific compounds (I) are disclosed e.g. 2-(4-fluorophenyl)-5-(N-(2-N,N-dimethylcarbamoyl)ethyl)piperidin-4-yl)-3-(4-pyridyl)pyrrole of formula (Ia).

EXAMPLE - A 2.0 M solution of lithium diisopropylamide in heptane, tetrahydrofuran (THF), ethylbenzene (3.1 ml) in THF (6 ml) at -78degreesC was treated dropwise with 4-picoline (0.5 g). The mixture was stirred for 20 minutes and a solution of 4-fluoro-(N-methyl-N-methoxy)-benzamide in THF (0.9 g) was added. The mixture was warmed to 0degreesC and worked up to give 1-(4-fluorophenyl)-2-(4-pyridinyl)-ethanone. A solution of the above compound (0.5 g) in dimethylsulfoxide (DMSO) (5 ml) was treated with 1 M sodium hexamethyldisilazide in THF (2.4 ml) and after 10 minutes a solution of 4-(2-iodoacetyl)-1-(benzyloxycarbonyl)-piperidine (0.72 g) in DMSO (1 ml) was added dropwise. After 2 hours, work up gave 4-(1-benzyloxycarbonylpiperidin-4-yl)-2-(4-pyridyl)-1-(4-fluorophenyl)-butane-1,4-dione (IV). A mixture (IV) and ammonium acetate (2 g) in acetic acid (5 ml) was heated at 110degreesC for 90 minutes. Work up gave 2-(4-fluorophenyl)-5-(1-benzyloxycarbonylpiperidin-4-yl)-3-(4-pyridinyl)-pyrrole (V). A solution of (V) (183 mg) in acetic acid (5 ml) was hydrogenated over 10% palladium on carbon (10 mg) for 25 hours to give 2-(4-fluorophenyl)-5-(piperidin-4-yl)-3-(4-pyridinyl)-pyrrole acetate salt (VI). A solution of (VI) (100 mg) and tert-butyl-(R)-(+)-4-formyl-2,2-

dimethyl-3-oxazolidine carboxylate (214 mg) in ethanol (15 ml) was treated with 8 M BH3.pyridine (0.12 ml) overnight. The crude product was purified by chromatography to give 5-(1-(2-amino-3-hydroxypropyl)-piperidin-4-yl)-2-(4-fluorophenyl)-3-(4-pyridyl)-pyrrole (61 mg).

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     (FILE 'HOME' ENTERED AT 09:55:45 ON 31 OCT 2007)

     FILE 'HCAPLUS' ENTERED AT 09:55:58 ON 31 OCT 2007
L1             1 SEA ABB=ON  PLU=ON  US20060240049/PN
                 D ALL

     FILE 'REGISTRY' ENTERED AT 09:57:38 ON 31 OCT 2007
L2             1 SEA ABB=ON  PLU=ON  DICLAZURIL/CN
                 D RN
L3             1 SEA ABB=ON  PLU=ON  101831-37-2
L4             1 SEA ABB=ON  PLU=ON  L2 OR L3
L5             1 SEA ABB=ON  PLU=ON  ETHANOL/CN
                 D RN
L6             1 SEA ABB=ON  PLU=ON  64-17-5/RN
L7             1 SEA ABB=ON  PLU=ON  L5 OR L6
                 E PEG-400/CN
L8             1 SEA ABB=ON  PLU=ON  SODIUM HYDROXIDE/CN
                 D RN
L9             1 SEA ABB=ON  PLU=ON  64-17-5/RN
L10            2 SEA ABB=ON  PLU=ON  L8 OR L9
L11            1 SEA ABB=ON  PLU=ON  ETHANOLAMINE/CN
                 D RN
L12            1 SEA ABB=ON  PLU=ON  141-43-5 /RN
L13            1 SEA ABB=ON  PLU=ON  L11 OR L12
L14            0 SEA ABB=ON  PLU=ON  TRIETHANYLAMINE/CN
                 E TRIE? (L) ANYLAMINE/CN
L15            0 SEA ABB=ON  PLU=ON  TRIETHANYL/CN
L16            1 SEA ABB=ON  PLU=ON  N-METHYLGLUCAMINE/CN
                 D RN
L17            1 SEA ABB=ON  PLU=ON  6284-40-8/RN
L18            1 SEA ABB=ON  PLU=ON  L16 OR L17
L19            1 SEA ABB=ON  PLU=ON  TPGS/CN
                 D IDE


     FILE 'STNGUIDE' ENTERED AT 10:05:48 ON 31 OCT 2007

     FILE 'HCA' ENTERED AT 10:07:21 ON 31 OCT 2007

     FILE 'HCAPLUS' ENTERED AT 10:07:26 ON 31 OCT 2007
L20          143 SEA ABB=ON  PLU=ON  DICLAZURIL/BI
L21          154 SEA ABB=ON  PLU=ON  L20 OR L4
L22       284893 SEA ABB=ON  PLU=ON  ETHANOL/BI
L23       332305 SEA ABB=ON  PLU=ON  L22 OR L7
L24         2847 SEA ABB=ON  PLU=ON  (PEG(W)400 OR PEG400 OR PEG-400 OR
                 POLYETHYLENEGLYCOL(W)400)/BI
L25         3389 SEA ABB=ON  PLU=ON  TOCOPHERYL/BI
L26            0 SEA ABB=ON  PLU=ON  L24(W)L25
L27            7 SEA ABB=ON  PLU=ON  L24 (L) L25
L28            0 SEA ABB=ON  PLU=ON  TOCOPHERYL PEG/OBI(W)400/BI
L29          509 SEA ABB=ON  PLU=ON  N/OBI(W)METHYLGLUCAMINE/BI
L30        99844 SEA ABB=ON  PLU=ON  SODIUM HYDROXIDE/BI
L31        26353 SEA ABB=ON  PLU=ON  ETHANOLAMINE/BI
L32            1 SEA ABB=ON  PLU=ON  TRIETHANYLAMINE/BI
L33         1528 SEA ABB=ON  PLU=ON  L29 OR L18
L34       325195 SEA ABB=ON  PLU=ON  L10 OR L30
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L35       41162 SEA ABB=ON  PLU=ON  L13 OR L31
L36         701 SEA ABB=ON  PLU=ON  ANTI/OBI(W)PROTOZOAL?/OBI OR ANTIPROTOZOAL?
                /OBI
L37        4809 SEA ABB=ON  PLU=ON  (PROTOZOAL/OBI OR CENTRAL NERVOUS SYSTEM?/O
                BI OR CNS/OBI OR CEREBRAL PROTOZOAL/OBI) (W) (INFECT?/OBI OR
                DISEASE?/OBI)
L38         210 SEA ABB=ON  PLU=ON  L36 (L) (AGENT?/OBI)
                E DICLAZURIL PROTOZOACIDE/CT
L39           9 SEA ABB=ON  PLU=ON  L21 AND (L36 OR L37 OR L38)
L40          11 SEA ABB=ON  PLU=ON  L21 AND (L23 OR L24)
L41           0 SEA ABB=ON  PLU=ON  L40 AND (L24)
L42           0 SEA ABB=ON  PLU=ON  L40 AND L25
L43          10 SEA ABB=ON  PLU=ON  L21 AND (L33 OR L34 OR L35)
L44           6 SEA ABB=ON  PLU=ON  L40 AND L43
                D SCAN TI HIT
L45           3 SEA ABB=ON  PLU=ON  L39 (L) (L40 OR L43)
L46           3 SEA ABB=ON  PLU=ON  L39 (P) (L40 OR L43)
                D SCAN TI HIT
L47        4034 SEA ABB=ON  PLU=ON  PROTOZOACIDE?/BI
L48          25 SEA ABB=ON  PLU=ON  L47 AND L21
                E ALCOHOLS/CT
L49      156714 SEA ABB=ON  PLU=ON  ALCOHOLS/CT
L50       29739 SEA ABB=ON  PLU=ON  L49 (L) (THU OR BIOL)/RL
                E SOLVENTS/CT
L51       60391 SEA ABB=ON  PLU=ON  SOLVENTS/CT
L52          43 SEA ABB=ON  PLU=ON  L51 (L) (THU OR BIOL)/RL
                E EMULSIFIERS/CT
L53       26448 SEA ABB=ON  PLU=ON  "EMULSIFYING AGENTS"/CT
L54          58 SEA ABB=ON  PLU=ON  L53 (L) (THU OR BIOL)/RL
L55          46 SEA ABB=ON  PLU=ON  L47 AND L50
L56           7 SEA ABB=ON  PLU=ON  L55 AND L51
L57           0 SEA ABB=ON  PLU=ON  L56 AND L54
L58       45011 SEA ABB=ON  PLU=ON  EMULSIFIER?/BI
L59           2 SEA ABB=ON  PLU=ON  L56 AND L58
                D SCAN TI HIT
L60           1 SEA ABB=ON  PLU=ON  L56 AND (L36 OR L37)
L61           2 SEA ABB=ON  PLU=ON  L59 OR L60
L62           4 SEA ABB=ON  PLU=ON  L45 OR L61
                E DE SPIEGELEER B/AU
L63          43 SEA ABB=ON  PLU=ON  ("DE SPIEGELEER B"/AU OR "DE SPIEGELEER B
                M"/AU OR "DE SPIEGELEER B M J"/AU OR "DE SPIEGELEER BART"/AU
                OR "DE SPIEGELEER BART M J"/AU)
                E DOSOGNE H/AU
L64          24 SEA ABB=ON  PLU=ON  ("DOSOGNE H"/AU OR "DOSOGNE HILDE"/AU)
L65           2 SEA ABB=ON  PLU=ON  L63 AND L64
L66          65 SEA ABB=ON  PLU=ON  L63 OR L64
L67           1 SEA ABB=ON  PLU=ON  L66 AND (L36 OR L37)
L68           1 SEA ABB=ON  PLU=ON  L66 AND L21
L69           2 SEA ABB=ON  PLU=ON  L65 OR L67 OR L68
L70           1 SEA ABB=ON  PLU=ON  L69 NOT L62
                D TI
                D AU
                SAVE TEMP L62 JAV162HCAP/A
                SAVE TEMP L70 JAV162HCAIN/A

    FILE 'WPIX' ENTERED AT 10:35:50 ON 31 OCT 2007
L71          30 SEA ABB=ON  PLU=ON  L20 OR L4
L72          11 SEA ABB=ON  PLU=ON  L71 AND (L36 OR L37)
                D SCAN TI HIT
L73           2 SEA ABB=ON  PLU=ON  L72 AND (L22 OR PEG(W)400 OR PEG400 OR
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                PEG-400 OR POLYETHYLENEGLYCOL(W)400 OR N-METHYLGLUCAMINE OR
                SODIUM HYDRIDE OR ETHANOLAMINE OR TRIETHANYLAMINE)
                D SCAN
                SAVE TEMP L73 JAV162WPIX/A

     FILE 'MEDLINE, BIOSIS, BIOTECHNO, DRUGU, EMBASE' ENTERED AT 10:40:18 ON
     31 OCT 2007
L74          320 SEA ABB=ON  PLU=ON  L21
L75         2762 SEA ABB=ON  PLU=ON  (PEG(W) 400 OR PEG400 OR PEG-400 OR
                 POLYETHYLENEGLYCOL(W) 400)
L76          390 SEA ABB=ON  PLU=ON  TOCOPHERYL PEG(W) 400 OR TPGS
L77        48904 SEA ABB=ON  PLU=ON  (N(W) METHYLGLUCAMINE OR SODIUM HYDROXIDE
                 OR ETHANOLAMINE OR TRIETHANYLAMINE)
L78            0 SEA ABB=ON  PLU=ON  L74 AND L75
L79            0 SEA ABB=ON  PLU=ON  L74 AND L76
L80            3 SEA ABB=ON  PLU=ON  L74 AND L77
                 D SCAN
                 D TI KWIC 1-3
L81       703155 SEA ABB=ON  PLU=ON  ALCOHOL?
L82        25690 SEA ABB=ON  PLU=ON  EMULSIF?
L83       452250 SEA ABB=ON  PLU=ON  FATTY ACID?
L84            0 SEA ABB=ON  PLU=ON  L21 AND L81
L85            0 SEA ABB=ON  PLU=ON  L21 AND L82
L86            1 SEA ABB=ON  PLU=ON  L21 AND L83
                 D SCAN
                 D TI KWIC
L87          100 SEA ABB=ON  PLU=ON  L21 AND (L36 OR L37)
L88            0 SEA ABB=ON  PLU=ON  L87 AND L81
                 D TI KWIC 3-5 L87

     FILE 'HCAPLUS' ENTERED AT 10:49:08 ON 31 OCT 2007
L89          301 SEA ABB=ON  PLU=ON  L23 AND L24
L90          233 SEA ABB=ON  PLU=ON  L89 AND (L33 OR L34 OR L35 OR L32)
L91            0 SEA ABB=ON  PLU=ON  L90 AND (L36 OR L37)
L92            0 SEA ABB=ON  PLU=ON  L90 AND L21
L93            0 SEA ABB=ON  PLU=ON  L47 AND L90
L94            0 SEA ABB=ON  PLU=ON  PROTOZOAL?/OBI AND L90
L95            0 SEA ABB=ON  PLU=ON  PROTOZOAL?/BI AND L90

     FILE 'MEDLINE, BIOSIS, BIOTECHNO, DRUGU, EMBASE' ENTERED AT 10:52:07 ON
     31 OCT 2007
L96           68 SEA ABB=ON  PLU=ON  DE SPIEGELEER B/AU
L97           14 SEA ABB=ON  PLU=ON  DE SPIEGELEER BART/AU
L98           12 SEA ABB=ON  PLU=ON  DOSOGNE HILDE/AU
L99           60 SEA ABB=ON  PLU=ON  DOSOGNE H/AU
L100           0 SEA ABB=ON  PLU=ON  L96 AND L99
L101           1 SEA ABB=ON  PLU=ON  L97 AND L98
                 D TI
L102          25 SEA ABB=ON  PLU=ON  L97 OR L98
L103           0 SEA ABB=ON  PLU=ON  L102 AND PROTOZOAL?
L104           0 SEA ABB=ON  PLU=ON  L102 AND L21
L105          11 SEA ABB=ON  PLU=ON  L102 AND (PHARMAC? OR THERAP? OR TREAT?)
                 D TI KWIC 3-7
L106          12 SEA ABB=ON  PLU=ON  L101 OR L105
                 SAVE TEMP L106 JAV162MULTIN/A

     FILE 'WPIX' ENTERED AT 10:56:22 ON 31 OCT 2007
L107           3 SEA ABB=ON  PLU=ON  L96 OR L97
L108           1 SEA ABB=ON  PLU=ON  L98 OR L99
L109           3 SEA ABB=ON  PLU=ON  L107 OR L108
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                D TI AU 1-3
                SAVE TEMP L109 JAV162WPIN/A

     FILE 'STNGUIDE' ENTERED AT 10:58:37 ON 31 OCT 2007
                D QUE L70
                D QUE L109
                D QUE L106

     FILE 'HCAPLUS, MEDLINE, BIOSIS, WPIX' ENTERED AT 11:03:55 ON 31 OCT 2007
L110          13 DUP REM L70 L106 L109 (3 DUPLICATES REMOVED)
                     ANSWER '1' FROM FILE HCAPLUS
                     ANSWERS '2-7' FROM FILE MEDLINE
                     ANSWERS '8-10' FROM FILE BIOSIS
                     ANSWERS '11-13' FROM FILE WPIX
                D L110 1-13 IBIB AB
                D QUE L62
                D QUE L73
L111           5 DUP REM L62 L73 (1 DUPLICATE REMOVED)
                     ANSWERS '1-4' FROM FILE HCAPLUS
                     ANSWER '5' FROM FILE WPIX
                D L111 1-4 IBIB ED ABS HITIND
                D L111 5 IALL ABEQ TECH ABEX
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